

## WHAT IS CLAIMED IS:

## 1. A biosensor comprising:

(a) a substrate in contact with a culture medium capable of supporting metabolism of at least one electrically excitable cell;

5 (b) a cell network composed of at least one of said electrically excitable cells, which cell has a predefined polarity on said substrate and is capable of producing a signal in response to a bioeffecting substance; and

10 (c) at least one signal transducer operably coupled to said cell network, which transducer is capable of detecting said signal produced in said cell network.

2. The biosensor of claim 1, wherein the signal produced by said cell network is an action potential, axonal wave potential, or dendritic wave potential.

15 3. The biosensor of claim 1, wherein the cell is a spinal cord cell, hippocampal cell, CNS excitatory cell line, or a cell line derived from stem cells.

20 4. The biosensor of claim 1, wherein said defined polarity is defined by a pattern of a self-assembled monolayer or biological macromolecule present on the surface of said substrate.

5. The biosensor of claim 1, wherein the transducer is a field effect transistor or a microelectrode.

6. The biosensor of claim 1, further comprising an insulating and/or barrier layer interposed between said at least one transducer and said culture medium, which insulating and/or barrier layer prevents direct contact between the culture medium and the transducer.

7. The biosensor of claim 6, wherein said insulating and/or barrier layer is selected from the group consisting of silica, silicon, germanium, gallium, arsenide, epoxy resin, polystyrene, polysulfone, aluminum, platinum, alumina, silicone, fluoropolymers, polyesters, acrylic copolymers, polyglactin, and polylactates.

8. The biosensor of claim 7, wherein the insulating and/or barrier layer comprises silica, silicon nitride, or silicon carbide.

9. The biosensor of claim 1, wherein said substrate has a patterned surface with at least one region thereon having an exposed surface of at least one cell adhesion promoter or cell adhesion inhibitor, which region is spatially related to the transducer so that a cell adhering to said region may be stimulated or detected by said transducer.

10. The biosensor of claim 9, wherein said cell adhesion promoter contains a terminal group selected from the group consisting of  $-NHCH_2CH_2NHCH_2CH_2NH_2$ ,  $-NHCH_2CH_2NH_2$ , 11-aminoundecyl, 3-aminopropyl, 3-(1-aminopropoxy)-3,3-dimethyl-1-propenyl, 6-(aminohexyl)propyl,

N-(2-aminoethyl)-3-aminopropyl,  $-(\text{CH}_2)_3\text{-NH-}(\text{CH}_2)_3\text{-NH-}(\text{CH}_2)_3$ ,  
 Gly-Arg-Gly-Asp-Tyr-, and Gly-Tyr-Ile-Gly-Ser-Arg-Tyr.

11. The biosensor of claim 9, wherein said cell adhesion inhibitor  
 5 is selected from the group consisting of  
 tridecafluoro-1,1,2,2-tetrahydrooctyl)-1-dimethylchlorosilane,  
 tridecafluoro-1,1,2,2-tetrahydrooctyl)-1-trichlorosilane,  
 tridecafluoro-1,1,2,2-tetrahydrooctyl)-1-methyldichlorosilane,  
 tridecafluoro-1,1,2,2-tetrahydrooctyl)-1-triethoxysilane,  
 10 (3,3,3-trifluoropropyl)trichlorosilane,  
 (3,3,3-trifluoropropyl)methyldichlorosilane,  
 (3,3,3-trifluoropropyl)-dimethylchlorosilane,  
 (3,3,3-trifluoropropyl)methyldimethoxysilane,  
 (3,3,3-trifluoropropyl)trimethoxysilane, (heptafluoroisopropoxy)  
 15 propylmethyldichlorosilane, (3-pentafluorophenylpropyl)  
 dimethylchlorosilane, polyethylene glycols, silanes having a  
 branched or unbranched  $\text{C}_3\text{-C}_{40}$  alkyl terminus, phenyl groups, and  
 inhibitory biological macromolecules.

12. The biosensor of claim 1, wherein a gigaohm seal is provided  
 20 between the cell and the substrate.

13. The biosensor of claim 1, wherein a self-assembled monolayer is  
 provided on the substrate in a predefined pattern, and the neuron  
 is provided thereon.

14. The biosensor of claim 13, wherein a cell-repulsive surface is provided at the periphery of the self-assembled monolayer.

15. The biosensor of claim 13, wherein the self-assembled monolayer is composed of trimethoxysilylpropyl diethylene tetraamine (DETA).

5 16. The biosensor of claim 1, wherein said cell is a hippocampal neuron.

17. The biosensor of claim 1, wherein said transducer is capable of stimulating said electrically excitable cell.

10 18. The biosensor of claim 1, wherein the transducer is formed in the substrate.

19. A biosensor comprising:

a substrate;

first and second neurons provided on at least a portion of the substrate, said neurons each having a predefined polarity;

15 a first transducer adjacent one of said neurons and capable of detecting a signal therein; and

a second transducer adjacent one of said neurons and capable of stimulating or detecting a signal therein, said neurons being in synaptic relationship so that a signal established in one of the  
20 neurons is attenuated by the other neuron.

20. The biosensor of claim 19, further comprising a stimulator adjacent one of said first and second neurons, which upon stimulation is capable of affecting a signal established therein.

5 21. The biosensor of claim 19, wherein said first and second transducers are microelectrodes.

22. The biosensor of claim 19, wherein said first and second transducers are field effect transistors.

23. A method of detecting a bioeffecting substance in a test sample, comprising:

10 (a) providing said test sample and a biosensor as in claim 1, wherein at least one cell of said biosensor produces a detectable response to said bioeffecting substance;

(b) contacting the test sample with the biosensor;

15 (c) monitoring, with a transducer of the biosensor, a signal produced by said at least one cell in response to contacting said cell with the test sample; and

(d) correlating said signal to the presence or absence of said bioeffecting substance in the test sample.

20 24. The method of claim 23, wherein the biosensor comprises at least two transducers.